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08/938,548

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/938,548	09/26/97	BERGSMA	D 61650037-2

EXAMINER

HM21/0923

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ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 09/23/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 7/17/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-16 is/are pending in the application.
Of the above, claim(s) 2,3,5-12,15+16 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1,4+13-14 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s): _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

Drawings

1. The drawings submitted with this application were declared informal by applicant. Accordingly they have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review. Direct any inquires concerning drawing review to the Drawing Review Branch (703) 305-8404.

Election/Restriction

2. Claims 2, 3, 5-12 and 15-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected inventions. Election was made **without** traverse in Paper No. 7, mailed July 20, 1998.

Double Patenting

3. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 3, 13 and 14 (as drawn to rat ligands SEQ ID Nos: 2, 3, 6, 8, 9 and 11) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4 and 13 of copending Application No. 08/820,519 which claim polypeptide ligands drawn to the rat sequence corresponding to SEQ ID NOs: 2, 8 and 9 of the instant application. It is noted that applicant admits that SEQ ID NO:3, 8, and 11 are identical in the human, rat and mouse species and therefore the disclosure of the rat in the '519 application renders obvious the instant claims which are drawn to a Markush which includes the sequences of the '519 application.. Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim SEQ ID NOs which overlap the Markush groups and species claimed in the earlier filed application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

6. Claims 1, 4, 13, and 14 are rejected under 35 U.S.C. 101 because: the claimed invention is directed to non-statutory subject matter. In the instant case the polypeptides are deemed a product of nature and the language of the claims fails to recite language such as "isolated and purified" which would indicate the "hand of man" in the production or manufacture of the product *per se*.

Claim Rejections - 35 USC § 112

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 2, 3, 4, 6, 8, 9, 10, 11 and 12 which corresponds to the human, rat and mouse species of HFGAN72 receptor ligand proteins. These SEQ ID NOs meet the written description provision of 35 USC 112, first paragraph. However, the claims are directed to or encompass sequences that have a recited degree of identity. None of these sequences meets the written description provision of 35 USC 112, first paragraph because the specification fails to recite the particular algorithm and parameters used to compare the two sequences. The scoring method (i.e. the algorithm and specific parameters) will determine the specific outcome (i.e. percent identity of any two sequences). Thus, in the absence of a written description of the algorithm and specific parameters employed the specification lacks adequate written description of sequences encompassed by percent identity language.

With the exception of the specific SEQ ID NOs, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, the only specific but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

8. Claims 1, 4, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The scope of the claims are drawn to an polypeptides comprising an amino acid sequence which is at least 80% identical over its entire length to an amino acid sequence selected from the group consisting of SEQ ID NO:2, 3, 4, 6, and 8-12 and polypeptides comprising SEQ ID NO:2, 3, 4, 6, and 8-12. The written description of the polypeptide is limited to the HFGAN72 receptor ligand protein sequence SEQ ID NO:2, 6, and 10 which encodes subsequences SEQ ID NO:3, 4, 8, 9, 11 and 12, wherein the protein subsequences have been identified to function as a HFGAN72 ligand which binds to the HFGAN72 orphan receptor.

As to claim 1, the specification fails to provide an enabling specification of any other polypeptides within the 80% identical, which function equivalently to the disclosed SEQ ID NOs in the activity assays of the invention. The activity assay of the invention requires a cell transfected with the HFGAN72 receptor, however the specification fails to teach how to identify the DNA

encoding the HFGAN72 receptor, how to transfect the cells and what its structural or functional identity is such that one of skill in the art could reproduce the screening assay of the invention. The recitation of receptor by name fails to provide sufficient information to the skilled artisan such that the appropriate DNA could be identified and transfected to even begin to screen for identity variants or homologs. The HFGAN72 orphan receptor is not described in the specification. The HFGAN72 receptor has no known art accepted equivalents, nor is published in the art such that one of skill in the art would be readily apprised of what receptor HFGAN72 represents. The specification fails to provide written description of the DNA encoding the receptor such that the skilled artisan would know how to make transfectants using DNA in order to screen for variants. Thus, the specification fails to teach how to screen for polypeptides having at least 80% identity from any other polypeptide that possesses not of the desired functions of the instant invention. The specification fails to provide an enabling written description of any variant, derivative or homolog the particularly claimed sequence identifiers. The specification fails to how to screen for other mammalian homologs or variants which would have the identical functional properties as the ligands of the invention. Thus, one of skill in the art would be reduced to merely randomly altering amino acid(s) which would lead to unpredictable results regarding the functional activity of the protein. Protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted *a priori* and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position

118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3):1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein.

In regard to claims 1, 4, 13 and 14, the specification provides no guidance as to "how to use" the polypeptides of the instantly claimed SEQ ID NOs because it is not known or disclosed what diagnostic or clinical use these polypeptides have. The specification alleges that the ligands provide for a diagnostic or therapeutic use. However, the specification provides no disease which has aberrant levels of the ligand such that it could in fact be diagnostic of any disease or be administered to provide a treatment. Moreover, no assays are described by which one of ordinary skill in the art could extrapolate as to what constitutes the unique biological and functional characteristics of the ligand-receptor pair. Assuming merely for arguments sake that one could screen, the specification fails to teach what physiological and biological activity is affected by the ligand binding to the HFGAN72 orphan receptor such that one skilled in the art would be readily apprised of how to use the ligand for therapeutic purposes. The specification teaches that calcium currents are generated by the SEQ ID NOs, however calcium release is a property of multiple disparate receptors with multiple different biological effects and does not distinguish the physiological and biological activity of the receptor HFGAN72. The specification fails to teach what disease are associated with either an increase or decrease of the ligand per

se, such that one of skill would be readily apprised of how to use the ligand levels for a diagnostic.

In view of the lack of specific written description of conception of protein homologs, the lack of an enabling written description of how to obtain, make and use the proteins comprising the instantly claimed SEQ ID NOs or homologs having at least 80% sequence identity to the SEQ ID NOs, the unpredictability associated with producing and using the myriad of homologs encompassed in the scope of the claims, the lack of an appropriate screening assay lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation to practice (i.e. make and use) the invention as is broadly claimed.

9. Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1 and 4, the claims are confusing because applicant admits in the specification that SEQ ID Nos: 3, 8 and 11 are identical for human rat and mouse respectively and thus the recitation of identical sequences by different SEQ ID NOs is redundant in the claims.

As to claims 1 and 4, the claims form an improper Markush group including hyphens, thus it is unclear as to the subject matter encompassed. The examiner presents the following claim language for applicants consideration. This language would obviate the above recited second paragraph rejections. -- An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:10 and SEQ ID NO:12.--

As to claim 1, the recitation of "at least 80% identical over its entire length" is vague and indefinite in the absence of a clear description or definition of what the term means. The percent identity as compared to a prototypical sequence depends both on the algorithm used and the specific parameters (i.e. mismatch penalty, gap penalty, gap size penalty or joining penalty) set by the user of the algorithm, such parameters are not set forth in the specification and thus the metes and bounds of the phrase "at least 80% identical over its entire length" can not be determined.

Status of Claims

10. No claims are allowed.

11. Claims 1, 4, 13 and 14 are free of the prior art.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Patricia A. Duffy, Ph.D.
September 21, 1998

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600